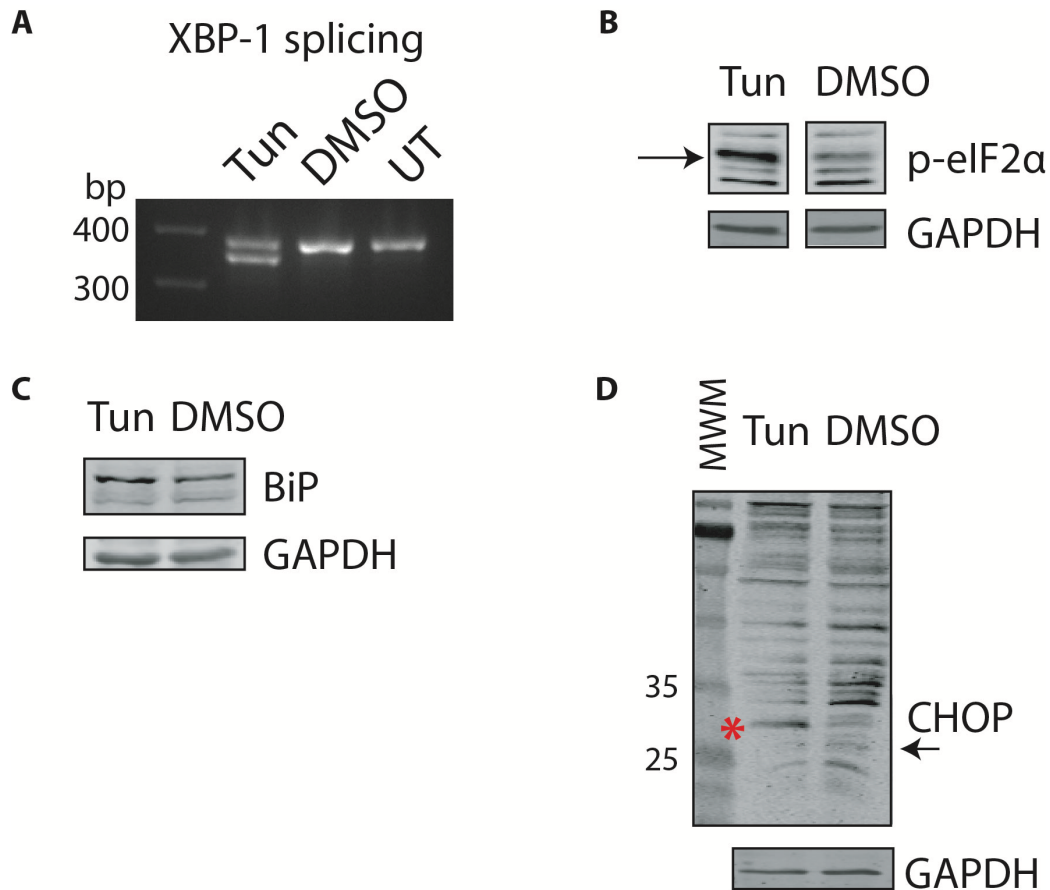
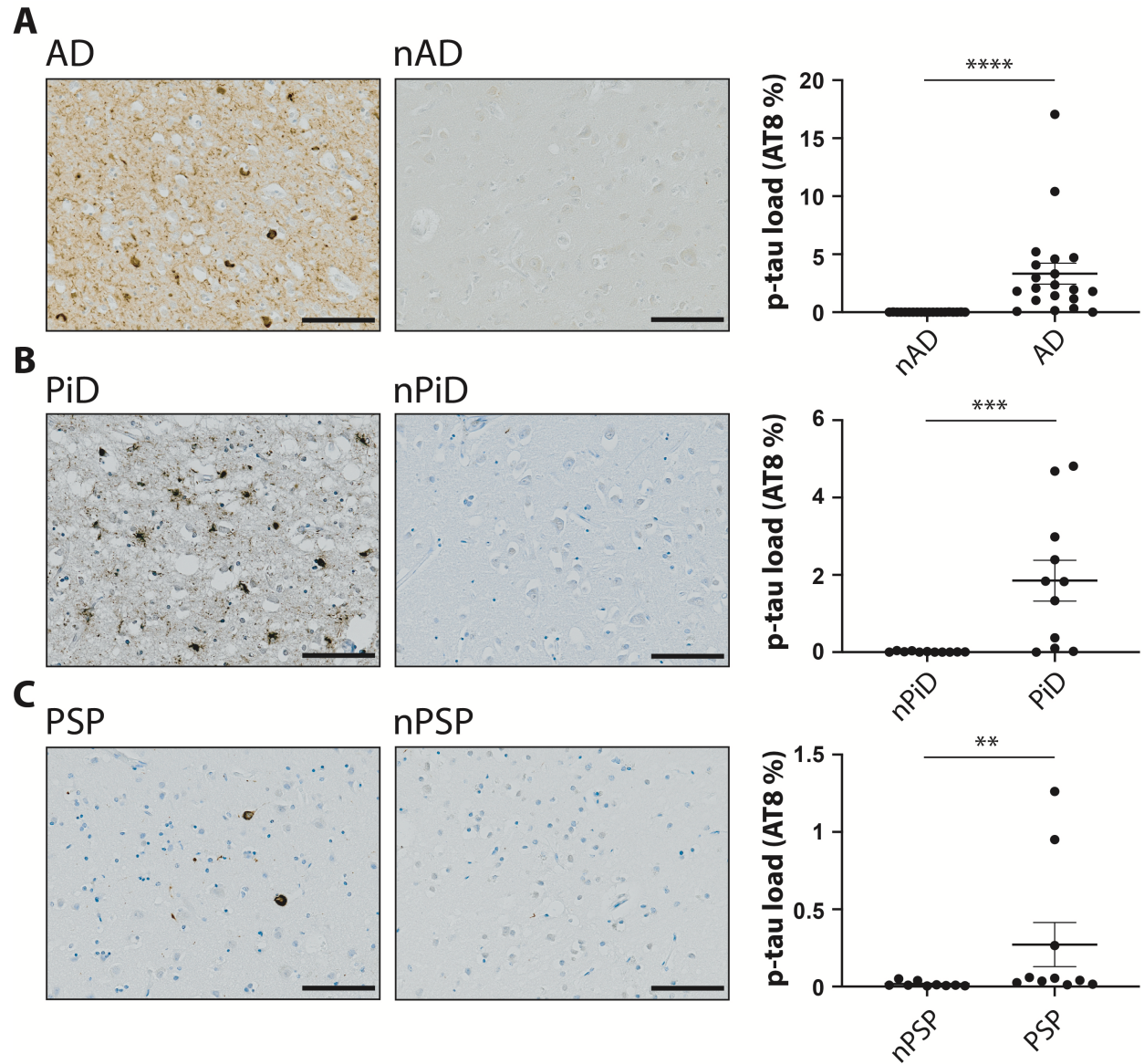


Supplementary Material

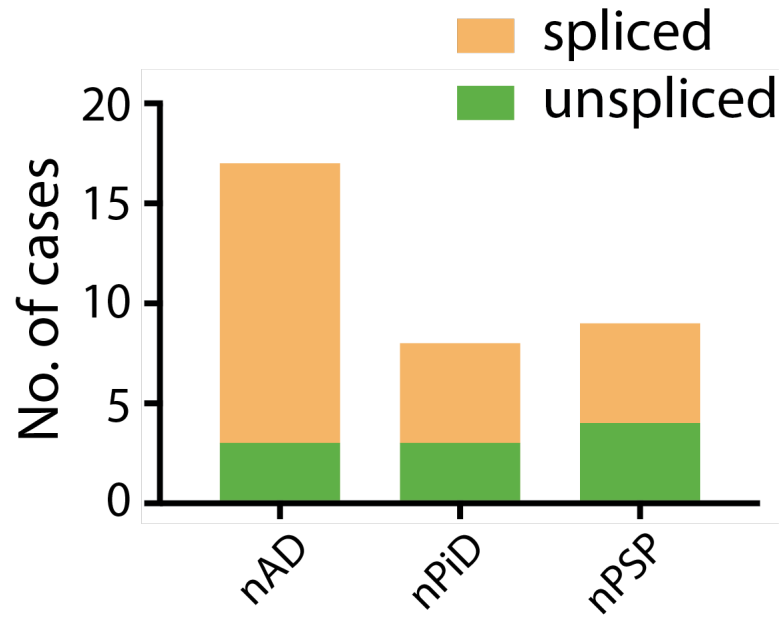
Molecular Investigation of the Unfolded Protein Response in Select Human Tauopathies



Supplementary Figure 1. Benchmarking reagents for their ability to resolve UPR in human samples. mRNA and protein were extracted from tunicamycin (Tun, 2 μ g/ml)- treated or DMSO (0.1%)-treated cells for 2 (for XBP-1 splicing), 3 (for p-eIF2 α detection), or 6 h. A) cDNA from HEK cells showed selective induction of XBP-1 splicing following tunicamycin treatment. B) Modest induction of eIF2 α phosphorylation in tunicamycin-treated samples. The samples were reprobed for GAPDH immunoreactivity. C) BiP protein expression (normalized to GAPDH) is selectively induced in HEKs treated with tunicamycin. D) CHOP protein expression (normalized to GAPDH) is selectively induced in HEKs treated with tunicamycin. Non-specific bands can be observed after the incubation with CHOP antibody that can be seen on the full blot presented. However, tunicamycin treatment leads to the induction of a protein of expected size (indicated with red asterisk) and this band was used for CHOP protein quantification. The arrow indicates the unspecific band that is also highlighted in Fig. 5 with an arrow. Molecular weight marker (MWM) highlighting 35 and 25 kDA bands is shown as a reference.



Supplementary Figure 2. Representative images of p-tau staining in brain samples from distinct tauopathy cohorts. A) AD and age-matched controls nAD, B) PiD and age-matched nPiD, C) PSP and age-matched nPSP samples were stained with AT8. The quantification of AT8 staining was analyzed using a Mann-Whitney test. Shown is the mean, error bars are SEM. **** $p < 0.0001$, $U = 9$ (AD); *** $p = 0.0006$, $U = 11$ (PiD); ** $p = 0.0021$, $U = 9$ (PSP). Scale bar indicates 100 μm .



Supplementary Figure 3. XBP-1 splicing occurs independently of tauopathy. Representation of number of cases that exhibited XBP-1 splicing/lack of splicing within the non-demented cohorts studied. There are no statistically significant differences between the cohorts in terms of XBP-1 splicing (Fisher's exact test).